REMARKS

Claims 83, 86 and 87 were pending in this application. Claim 83 was rejected. Claims 86 and 87 are cancelled as being drawn to a nonelected invention. Claim 83 has been amended to limit the claim to the protein of SEQ ID NO:5, the elected species. The amendment does not add any additional matter. Reconsideration of the claim in view of the following comments is respectfully requested.

Applicants have carefully considered the points raised in the Final Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Withdrawn Objections and Rejections

Applicants acknowledge that the Office has withdrawn the objections to the specification, has entered the substitute specification and replacement drawings in full, has withdrawn the rejection of claims 83-85 as indefinite, has withdrawn the rejection of claims 83-85 as lacking written description, has withdrawn the rejection of claim 84 for lack of enablement, and has withdrawn the rejection of claims 83-84 as anticipated. Applicants gratefully acknowledge that the claims were found to be free of the prior art.

Claim 83 currently stands rejected only for lack of enablement.

Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

Claim 83 was rejected for lack of enablement. The Office asserted that "while the claims are not broad in scope, the present application does not provide sufficient enablement for a transcript variant encoding the protein of SEQ ID NO:5." (OA at page 3). The Office further asserted that Applicants have "not taught how to make and/or use (i) . . . the protein of SEQ ID NO:5 encoded by the presently claimed transcript variant, or (ii) the structural and functional characteristics of . . . the protein of SEQ ID NO:5 encoded by the presently claimed transcript variant." (OA at page 4). Specifically, the Office stated that Applicants have "not provided

sufficient biochemical information (e.g. structural characteristics, amino acid composition, physicochemical properties, etc) that distinctly identifies (i) . . . the protein of SEQ ID NO:5 encoded by the presently claimed transcript variant, or (ii) the structural and functional characteristics of . . . the protein of SEQ ID NO:5 encoded by the presently claimed transcript variant. The specification does not provide sufficient guidance as to which isolated 121P1F1-related protein or any fragment of said protein would share the same function as the 121P1 F1 protein of SEQ ID NO:2. Neither does the specification provide any working examples of any 121 P1 F1-related protein (i.e., SEQ ID NO:5) that have the same functional activities or characteristics, i.e., highly expressed in prostate cancer as the 121 P1 F1 protein." The Examiner also cited a number of articles that allegedly teach that it is inappropriate to assign a functional activity based on sequence homology. Applicants respectfully traverse this rejection.

The Examiner is essentially asserting that there is no objective evidence that all or any of the transcript variants specified in the claims possess the same properties as the generic 121P1F1 sequence, such that the transcript variants are over-expressed in cancers.

Applicants respectfully note that genetic variation between the sequences does not necessarily imply that each variant has a unique function. Moreover, the biological function of the individual protein variants is irrelevant to the use of the claimed proteins as a family of markers for the detection of cancer by monitoring expression levels in test tissues.

The scope of enablement must only bear a "reasonable correlation" to the scope of the claims. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); MPEP § 2164.08. All that is required to show enablement under 35 U.S.C. § 112, first paragraph, is that a person skilled in the art could make and use the claimed invention without undue experimentation.

In the present case, the pending claims are directed to a novel transcript variant of a protein (121P1F1) disclosed in the application. Applicants have asserted in the application that the claimed sequences have utility as diagnostic agents to identify prostate, bladder, kidney, colon, lung, pancreas, breast, cervix, and stomach cancer. Specification, page 5, paragraph **[0027]**, page

96, paragraph **[0373]**; Table I; and Figures 20 and 21. (All citations to the specification are based upon the substitute specification submitted April 4, 2007). The present application contains evidence that the novel gene which encodes the target protein expresses mRNA in cancer. "121P1F1 expression was seen in kidney, breast, cervix, and stomach cancers. 121P1F1 was also found to be highly expressed in a panel of cancer cell lines." Specification, page 11-12, paragraph **[0052]**; see also Figure 21. "121P1F1 expression was also shown in prostate cancer xenografts and in all cancer cell lines tested, such as in prostate . . . ; bladder . . . , kidney . . . ; colon . . . and in the cancer cell lines 293T, FE-Es and KCL.22". Specification, page 96, paragraph **[0093]**; see also Figures 17-19. The specification also shows that the target gene is expressed in normal testis and in thymus and ovary, but not in normal prostate. See Figure 18.

This is not a situation where the splice variant is unknown: the claimed sequence of the variant is disclosed as SEQ ID NO:5. The splice variant was identified by the use of EST data in an EST assembly approach. Specification, Example 5, page 99, paragraph **[0385]**. The specification further provides that the parameters of a splice variant can be confirmed using "a variety of techniques are available in the art, such as full-length cloning, proteomic validation, PCR-based validation, and 5' RACE validation, etc." Specification, page 99, paragraph **[0383]** (citations omitted). It is further known that genomic regions are modulated in cancers. When the genomic region to which 121P1F1 maps is modulated in a particular cancer, the splice variants of 121P1F1 are modulated as well. The specification thus provides that splice variants of 121P1F1 that are structurally and/or functionally similar to 121P1F1 – which was shown in the specification to have a particular expression profile – will share this expression pattern, and thus the splice variants can serve as tumor-associated markers/antigens. All of this data, taken as a whole, is more than sufficient to demonstrate that it is more likely than not to one of ordinary skill in the relevant art that the presently claimed invention is useful for the detection of cancers.

Moreover, the polynucleotide sequence encoding SEQ ID NO:5 is a naturally-occurring transcript variant of the nucleotide sequence comprising SEQ ID NO:1 that encodes SEQ ID NO:2. The specification provides ample disclosure with regard to expressing a 121P1F1 polypeptide in a host cell. For instance, Example 6, entitled "Production of Recombinant 121P1F1 in Prokaryotic

Systems," discloses protein expression in prokaryotic host cells and describes a number of expression vectors which may be employed therefor. Similarly, Example 7 and Figure 14 teach production of recombinant 121P1F1 in eukaryotic expression systems. Applicants also fully describe methods for generating polyclonal and monoclonal antibodies to 121P1F1. For example, Example 9, entitled "Generation of 121P1F1 Polyclonal Antibodies," discloses the generation of antibodies to 121P1F1 polypeptides or immunogenic portions thereof. The specification notably discloses the generation of a polyclonal antibody to the full-length 121P1F1 polypeptide. Figures 13 and 14 show that the "polyclonal antibody shows strong reactivity to MYC-HIS tagged 121P1F1 in transfected T cells and also to several proteins in the tumor cell lines, indicating reactivity to endogenous 121P1F1 and to variant molecules of different molecular weights." Specification, pages 111-112, paragraph **[0427]**; see also Figures 13 and 14. Figure 13 shows that the polyclonal antibody to 121P1F1 showed strong reactivity to variants of 121P1F1 in a number of cancer cell lines, including bone, bladder, lung, colon, and pancreatic cancer cell lines. Applicants have thus amply demonstrated that variants of 121P1F1 are expressed in cancer cells despite the differences in the amino acid sequences of the variants, and that those antibodies to 121P1F1 and/or its variants are thus useful as diagnostics.

With regard to claim 83, the Examiner alleged that Applicants have not shown a function for the protein. Applicants disagree. While they have not delved deeply into the biological role of 121P1F1 in living cells, Applicants have asserted the use of 121P1F1 and its variants as a marker for prostate cancer. What biological role the claimed protein plays in the life of a cell is not directly relevant to the question of patentability. All that the statute requires is that an Applicant "must teach those skilled in the art to make and use the full scope of the claimed invention without 'undue experimentation' ... Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). The specification clearly achieves this goal by disclosing the specific structure of the claimed variant, and .

Moreover, because the parent gene product has been patented (see, e.g., U.S. Patent No. 6,924,358 and USSN 11/125,805, Notice of Allowance mailed 08/07/2007), those of ordinary skill

in the art would be able to use variants of those patented sequences without undue experimentation. In view of the relationship between the claimed sequences and the issued and allowed U.S. patents, and the discussion above, Applicants request that the present rejection be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket **No. 511582003420**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: September 19, 2007

Respectfully submitted,

By: /Elizabeth Cary Miller/
Elizabeth Cary Miller
Registration No.: 54,708
Kate H. Murashige
Registration No.: 29,959
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
(858) 314-7717